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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/526,365 | 11/15/2005 | Roy Curtiss III | 56029-53712 | 9668 |

70119 7590 07/08/2010
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| EXAMINER |
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POPA, ILEANA

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| ART UNIT | PAPER NUMBER |
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1633

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| NOTIFICATION DATE | DELIVERY MODE |
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07/08/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPDOCKET@THOMPSONCOBURN.COM

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/526,365 | Applicant(s) CURTISS ET AL. | |
| | Examiner ILEANA POPA | Art Unit 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4,8,15,18,21 and 47-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4, 8, 15, 18, 21, and 47-64 is/are rejected.
- 7) ☒ Claim(s) 53 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/28/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of the invention of Group II, drawn to a host-vector system comprising two different regulatable promoters each repressed by a different repressor, in the reply filed on 12/08/2008 is acknowledged.

The applicant cancelled claims 1-3, 5-7, 9-14, 16, 17, 19, 20, and 22-46 and withdrew claims 21, 57-60, and 63.

Upon further consideration, **the restriction requirement between the inventions of Groups II and IV as set forth in the Office action mailed on 06/25/2008, is hereby withdrawn.** In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 4, 8, 15, 18, 21, and 47-64 are pending and under examination.

Specification

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2. The disclosure is objected to because of the following informalities: this application contains sequence disclosures (paragraph 201, Table 3) that are encompassed by the definitions for nucleotide sequences set forth in 37 CFR 1.821 (a)(1) and (d). However, the specification fails to comply with the requirements of 37 CFR 1.821 (a)(1) and (d), because the sequence identifiers, preceded by SEQ ID NO are missing.

Appropriate correction is required.

Claim Objections

3. Claim 53 is objected to because of the following informalities: the claim recites that “the terminator sequence is rrFG”. However, rrFG is the name of the gene encoding an *E. coli* ribosomal protein and not a sequence (see the instant specification, p. 86, paragraph 272). Appropriate correction to “wherein the terminator is the *rrFG* transcriptional terminator” is required.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d

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438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 4, 15, 18, 47-51, 54, 56 and 64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 11-13 of U.S. Patent No. 6,610,529. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to the same microorganism comprising the same host-vector system. The patent specification defines that the vector comprises a prokaryotic activator-promoter, an origin of replication, two regulatable promoters repressible by two different repressors, three transcriptional terminators, and a site for the insertion of genes of interest (see Fig. 4). Thus, the instant claims and the patent claims are obvious variants.

6. Claims 4, 15, 18, 21, 47-51, 56-60, and 62-64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 15, 19 and 24 of U.S. Patent No. 6,780,405. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to the same microorganism comprising the same host-vector system and to the same method of immunizing subjects by using the microorganism. The patent

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specification defines that the microorganism colonizes GALT (column 12, line 64 to column 13, line 19; column 30, lines 48-54). Although the patent claims do not recite a BAC vector, using such was routine in the prior art and it would have been within the knowledge and capabilities of one of skill in the art to use such when needed. Thus, the instant claims and the patent claims are obvious variants.

7. Claims 4, 15, 18, 47-51, 56-61, and 62-64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 21 of U.S. Patent No. 7,341,860. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to the same microorganism comprising the same host-vector system and to the same method of immunizing subjects by using the microorganism. The patent specification defines that the microorganism colonizes GALT (column 16, lines 1-17). Although the patent claims do not recite a BAC vector, using such was routine in the prior art and it would have been within the knowledge and capabilities of one of skill in the art to use such when needed. Thus, the instant claims and the patent claims are obvious variants.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 4, 15, 18, 21, 47-51, 54, and 56-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Curtiss et al. (WO 96/40947, applicant's IDS).

Curtiss et al. teach a microorganism comprising: **(i)** a chromosome comprising an inactivated *asd* gene, wherein the chromosome further comprises a nucleic acid encoding the C2 repressor operably linked to an arabinose-induced promoter; and **(ii)** a vector comprising an origin of replication, the *trc* promoter (i.e., a first regulatable promoter activated by a first repressor), the bacteriophage P22 P_R promoter (i.e., a second regulatable promoter activated by a second repressor), the bacteriophage P22 P_L promoter (i.e., a prokaryotic activator-promoter sequence) operably linked to the *asd* gene, a multicloning site wherein a gene of interest is inserted, and three transcription terminators (claims 4, 15, 47, 51, and 56) (p. 14, lines 3-21; p. 16, lines 6-9; p. 31, line 25 through p. 32, line 10; p. 52; p. 58, lines 28-32; Fig. 13). Curtiss et al. teach using their microorganisms to deliver genes of interest to subjects such as to vaccinate the subjects, wherein the subjects are domestic birds such as chicken or humans, wherein the microorganisms colonize GALT, and wherein the genes of interest are from *Streptococcus pneumoniae* (claims 18, 21, 47-50, and 57-60) (p. 49, lines 10-14; p. 53, lines 1-21; p. 55, lines 7-17; p. 57, lines 5-9; p. 58, lines 15-18; p. 62, lines 20-30). Since Curtiss et al. teach all claim limitations, their teachings anticipate the claimed invention.

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Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 4, 15, 18, 21, 47-51, 54, 56-60, 62, and 63 are rejected under 35 U.S.C. 103(a) as being obvious over Curtiss et al., in view of Jenkins et al. (Poultry Science, 1991, 70: 539-547, Abstract).

The teachings of Curtiss et al. are applied as above for claims 4, 15, 18, 21, 47-51, 54, and 56-60. Although Curtiss et al. teach immunizing chicken, they do not specifically teach immunizing with an antigen from *Eimeria* (claims 62 and 63). However, vaccinating chicken with antigens derived from *Eimeria* was routine in the prior art (see Jenkins et al., Abstract). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Curtiss et al. by using an antigen derived from *Eimeria* to achieve the predictable result of inducing resistance to coccidiosis in chicken. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

12. Claims 4, 15, 18, 21, 47-54, and 56-61 are rejected under 35 U.S.C. 103(a) as being obvious over Curtiss et al., in view of both Guzman et al. (J Bacteriol, 1995, 177: 4121-4130) and Reddy et al. (Proc Natl Acad Sci USA, 1985, 82: 5656-5660).

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The teachings of Curtiss et al. are applied as above for claims 4, 15, 18, 21, 47-51, 54, and 56-60. Curtiss et al. do not teach mutating the *asd* gene by changing the ATG to TTG (claim 52). However, doing such is suggested by the prior art. For example, Curtiss et al. teach the necessity to eliminate possible leaky expression from their control sequences (p. 31, lines 14-24). Guzman et al. teach that regulatable promoters are leaky and express basal levels of proteins in their uninduced or repressed state, that basal expression levels for essential genes should be reduced to a minimum to ensure a proper control of gene expression, and that reduction of basal expression levels could take place by lowering the efficiency of initiation of translation (p. 4121, column 1; p. 4126, column 1; p. 4128, column 2, fourth full paragraph; p. 4129, column 1). Reddy et al. teach that replacing ATG with TTG reduces initiation of translation from regulatable promoters (Abstract). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the microorganism of Curtiss et al. by mutating the ATG to TTG in the essential gene *asd*, when leaky expression was encountered, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to achieve a better control of *asd* expression. One of skill in the art would have reasonably expected to be successful in doing so because the prior art teaches that replacing ATG to TTG is successful in limiting the initiation of translation.

Although Curtiss et al. teach transcription terminators (Fig. 13) and deletion of the *araBAD* operon (p. 32, lines 14-20), they do not specifically teach the *rrFG* transcription terminator (claim 53) or the specific Δ *araBAD1932* (claim 61). However, it

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is noted that there is no evidence on the record that the claimed *rrFG* transcription terminator or the $\Delta araBAD1932$ deletion result in a construct exhibiting an unexpected property. The terminator and the specific deletion are not significant if they do not provide a novel feature.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

13. Claims 4, 15, 18, 21, 47-51, 54, 56-60, and 64 are rejected under 35 U.S.C. 103(a) as being obvious over Curtiss et al., in view of Shizuya et al. (Proc Natl Acad Sci, USA, 1992, 89: 8794-8797).

The teachings of Curtiss et al. are applied as above for claims 4, 15, 18, 21, 47-51, 54, and 56-60. Curtiss et al. do not teach a BAC vector (claim 64). However, BAC vectors were routinely used in the prior art (see Shizuya et al., Abstract, p. 8794, column 1, p. 8796, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the microorganism of Curtiss et al. by using a BAC vector backbone to achieve the predictable result of obtaining a microorganism suitable for vaccination. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

14. Claims 4, 8, 15, 18, 21, 47-51, and 54-60 are rejected under 35 U.S.C. 103(a) as being obvious over Curtiss et al., in view of both Curtiss (U.S. Patent No. 4,190,495) and Oeschger et al. (U.S. Patent No. 4,337,314).

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The teachings of Curtiss et al. are applied as above for claims 4, 15, 18, 21, 47-51, 54, and 56-60. Curtiss et al. do not teach a vector system comprising two essential genes (claims 8 and 55). However, doing such is suggested by the prior art. For example, the prior art teaches using microorganism comprising two deletion affecting the synthesis of the rigid layer to prevent or diminish the probability that the microorganism would lose the property conferred by the deletion (see Curtiss, column 2, lines 24-30 and 60-63; column 4, lines 20-26; Oeschger et al., column 5, lines 20-25, column 7, lines 23-52, column 8, lines 13-20 and line 66 through column 9, line 8). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the microorganism of use two Curtiss et al. by introducing a second deletion of an gene essential for the synthesis of the rigid wall, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to obtain a microorganism wherein the probability of reversion is prevented or diminished. One of skill in the art would have reasonably expected to be successful in doing such because the prior art teaches routine experimentation to introduce such deletions into host microorganisms. It is noted that, by doing such, one of skill in the art would have necessarily provided the second essential gene on the same or on a different vector. With respect to a second desired product, one of skill in the art would have known to use a second antigen on the same or on a different vector, when vaccination against multiple antigens was needed. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

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15. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633